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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	**PAPER NUMBER**
1615	

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11/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/083,734	NEEDHAM, DAVID	
	Examiner	Art Unit	
	Gollamudi S Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57,59-64 and 66-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57,59-64 and 66-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 57,59-64,72,75,87-89,92,104,109,110,113-115,157 and 158.

DETAILED ACTION

The amendment dated 8-16-07 is acknowledged.

Claims included in the prosecution are 66-71, 73, 74, 76-83, 93, 97-103,116-156 and 159-169, 176-189.

Claim Rejections - 35 U.S.C. § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 66, 69, 77, 93, 97, 116-118, 121-122, 124-125, 128, 131-136 and 162-169 are rejected under 35 U.S.C. 102(b) as being anticipated by Eibl (5,626,867).

Eibl discloses liposomal formulations containing phospholipids. The phospholipids include DPPC and DSPA. One of the phospholipids, which could be used in combination, is a lysophosphatidic acid (either R1 or R2 in the structure on col. 2 is hydrogen). The liposomes contain a variety of active agents including anti-tumor agents (note the abstract, col. 1, line 65 through col. 2, line 43, col. 4, line 39 through line 61; Examples, example 1 in particular and claims).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Eibl merely describes a liposomal composition may include cholesterol, selective phospholipids and phosphatidic acid; applicant further argues that the reference also indicates that the preferred composition includes cholesterol and selected phospholipids. According to applicant, this combination does

not encompass the first and second component. This argument is not persuasive since instant claims do not exclude cholesterol and the reference teaches DPPC in combination with lysophosphatidic acid. .

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 66-71, 73, 74, 76-83, 93, 97-103,116-156 and 159-169, 176-189 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hristova (Macromolecules, vol. 28, pp. 7693-7699, 1995) in combination with Ogawa cited above.

Hristova discloses liposomal formulations containing dipalmitoylphosphatidylcholine and a lysolipid. The liposomes further comprise PEG derivatized lipids. Although Hristova does not teach instant lysolipid, monopalmitoylphosphatidylcholine, Hristova discusses the effect if lysolipids in general on gel phase bilayers and provides a specific example of the effect of the lysolipid, monooleoylphosphatidylcholine (note the abstract, Materials and Methods and Discussion). Therefore, it would have been obvious to one of ordinary skill in the art to use any lysophosphatidylcholine (that is substituted with any fatty acid moiety) with the expectation of obtaining similar effect on the gel phase bilayers. Hristova does not teach

specific encapsulated active agents or a method of administration using hyperthermia (heating). However, in the introduction part, Hristova clearly suggests that the liposomes are for drug delivery, though not using hyperthermia.

Ogawa as pointed out above, teaches that DPPC has a transition temperature of 41.4 degrees and the use of liposomes containing DPPC for hyperthermia therapy (note the abstract, col. 1, line 58 through col. 4, line 37; Examples and claims).

It would have been obvious to one of ordinary skill in the art to use liposomes containing DPPC of Hristova for the delivery of active agents by hyperthermia therapy with a reasonable expectation of success since Ogawa teaches that DPPC has a transition temperature of 41.4 degrees and liposomes containing this phospholipid could be used successfully for the delivery of active agents using hyperthermia therapy.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Hristova describes several combinations of materials on page 7695 that may be included in liposome bilayers, including DPPC. However, according to applicant, Hristova does not use hyperthermia and provides no description of drug delivery from the liposome. Applicant further argues that the only apparent description of a lysolipid bilayer is at page 7697 in which the reference recites incorporating mixtures of POPE-PEG:EPC:MOPC and that lysolipid and EPC form a liquid crystalline bilayer and not a gel-phase bilayer. These arguments are not persuasive. First of all, it is clear from the introduction section, Hristova studies various compositions keeping in mind the drug delivery nature of the liposomes. Although the combination taught by Hristova includes egg phosphatidylcholine, the motivation to use

a saturated phospholipid such as DSPC or DPPC could be derived from not only from the discussion by Hristova of the gel and liquid crystalline bilayers on page 7696, but also from Ogawa. If one of ordinary skill in the art desires to use the drug delivery using hyperthermia technique, he would be motivated to use a phospholipid with a higher transition temperature than the egg phosphatidylcholine in Hristova.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 66-71, 73, 74, 76-83, 93, 97-103,116-156 and 159-169, 176-189 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-68 of U.S. Patent No. 6,726,925. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims

in said patent and instant claims are drawn to the same compositions; in instant claims, the elected second component is lysolipid and the patented claims recite specific lysolipids; it would have been obvious to one of ordinary skill in the art to use any lysolipid with a reasonable expectation of success. Instant claims recite the active agent as a pharmacologically active agent, a flavor agent, a diagnostic agent or a nutritional agent whereas the patented claims recite a pharmacologically active agent or a diagnostic agent. The pharmacologically active agent and the diagnostic agent in instant application are anticipated by the patented claims. The flavor agent and nutritional agent are obvious variants since it would have been obvious to encapsulate any active agent in the liposomes in the patented claims since the principle of encapsulation is the same.

Applicant requests that the examiner hold the rejection in abeyance and therefore, the rejection is maintained in the absence of a terminal disclaimer.

7. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK